Remarks/Arguments:

Claims 1 to 4, 6 to 9, 23 to 26, 29 to 33, 35 to 39 and 71 to 77 are pending in the case. Claims 1 to 4, 6 to 9, 23 to 26, 29 to 33 and 35 to 39 have been amended to more clearly present the invention and differences between the amended claims and the previously pending claims should not be viewed as acquiescence to any of the Examiner's rejections. Claims 5, 10 to 22, 27, 28, 34 and 40 to 70 have been canceled and applicant reserves the right to pursue to canceled claims, for example, in one or more related applications.

Claim 26 has been amended to make claim 26 an independent claim thereby adding clarity to the claims. In addition, to clarify the claims, Claim 39 has been amended to indicate that the recombinant nucleic acid molecule comprises a bacterial artificial chromosome. To provide consistency, the claims have been amended to replace "according to" with "of".

New claims 77 and 78 have been added and are supported, for example, at page 20 lines 29 to 30, where it is stated that "One MAR element is 5' upstream of the ovalbumin gene, between about nucleotide positions 41701 and 41900" and at page 21, lines 2 to 3 where it is stated that "Another MAR element is between about 96401-96800". Applicant believes the present Response includes no new matter.

The Examiner reminds applicant that the status of the applications throughout the specification will need to be updated upon being allowed. Applicant will update the applications listed in the specification as is required.

The Examiner states that "Figure b" on page 43, line 23, does not exist. Applicant has amended the specification to eliminate reference to "Figure b".

The Examiner states that it appears that SEQ ID NO: 1 encodes BAC vector sequence as well as the ovalbumin gene and matrix attachment regions. SEQ ID NO: 1 does not include BAC vector sequence. In the assembly of sequence of SEQ ID NO: 1 from raw sequence data, a software program was used which is designed to omit vector sequence. In addition, in response to the Examiner's concern, a sequence homology search (BLAST search) was performed comparing the sequence of pECBAC1 (BAC vector backbone of BAC 120 and BAC 77) to SEQ ID NO: 1. The search confirmed SEQ ID NO: 1 does not encode BAC vector. The Examiner notes that in the Examples section an immunoglobulin coding sequence and luciferase coding sequence were inserted

into the 195 ovalbumin BAC. SEQ ID NO: 1 does not include immunoglobulin coding sequence or luciferase coding sequence.

The Examiner rejects claims 1 to 41 under 35 USC 112, second paragraph as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Applicant traverses the rejection.

The Examiner states that claims 1 to 3 and 27 and 28 are indefinite because the structural features that define chicken MARs vary and are not defined in the specification and are not known in the art. Applicant disagrees with the Examiner since many MAR sequences were known in the art at the time of filing. See, for example, references cited in the first and second full paragraphs of specification. In addition, the specification clearly discloses MAR sequences, for example, at page 20, lines 29 to 30, where it is stated that "One MAR element is 5' upstream of the ovalbumin gene, between about nucleotide positions 41701 and 41900" and at page 21, lines 2 to 3 where it is stated that "Another MAR element is between about 96401-96800". However, amendments to the claims have made the Examiner's rejection unnecessary since the rejected claims now refer to nucleotide sequence.

The Examiner rejects claims 10 to 22 indicating that the phrases "truncated variant" makes the claims unclear. Applicant disagrees with the Examiner. However, claims 10 to 22 have been canceled making the Examiner's rejection unnecessary.

The Examiner stated that the phrase "A vector inserted therein" in claims 23 and 34 does not make sense. Claim 23 has been amended and claim 34 has been canceled making the rejection unnecessary.

The Examiner points to a phrasing error in claim 25. Applicant has amended claim 25 in accordance with the Examiner's comments.

The Examiner rejects claims 27 and 28 because the claims do not clearly set forth the structure of the nucleic acid sequence. Applicant disagrees with the examiner. However, claims 27 and 28 have been canceled making the Examiner's rejection unnecessary.

The Examiner rejects claim 29 indicating that the term "heterologous" makes the claim unclear. Applicant disagrees with the examiner. However, claim 29 has been amended deleting the term "heterologous". Support for amended claim 29 is found, for example, at page 29, line 31 to page 30, line 1, where it is stated that "a first polypeptide-encoding region is operatively linked to an

avian ovalbumin promoter".

The Examiner rejects claim 30 stating that the metes and bounds of an endogenous nucleic acid sequence is unclear. Applicant disagrees with the examiner. However, claim 30 has been amended deleting the term "endogenous".

The Examiner states that the term "tissue-specific expression" is not art accepted and is not defined in the specification. Applicant disagrees with the Examiner since it is well known in the art that the term "tissue-specific expression" refers to gene expression with specificity for certain tissue. In fact, an internet Google search for "tissue-specific expression" brings up over one million hits indicating that "tissue-specific expression" is a well used and well known phrase in the art.

The Examiner has rejected claim 33 stating the claim does not make sense because the nucleic acid sequence does not have a first heterologous sequence and because "heterologous" does not make sense. Claim 33 has been amended deleting the term "heterologous and to depend from claim 29. Support for this amendment can be found, for example, at page 30 lines 2 to 3, where it is stated that "a second polypeptide-encoding region is operatively linked to an Internal Ribosome Entry Sequence (IRES)".

The Examiner rejects the claim 37 indicating that the claim is unclear since it cannot be determined what is being optimized or what is optimal regarding codon optimization. To add clarity, "complement" has been deleted from the claim. In addition, the meaning of codon optimization is well understood in the field of molecular biology and as such this rejection should be withdrawn. Codon optimization for the purpose of enhancing expression of a heterologous protein in a particular host cell was a concept well understood by those of skill in molecular biology at the time of this invention. For example, a person having ordinary skill in molecular biology would be able to envision what a codon is without a detailed definition and would understand that the coding sequence in an organism preferentially relies on certain codons to encode specific amino acid residues. Thus, a person of skill in the art would have no difficulty in interpreting the metes and bounds of "a codon optimized for protein expression in an avian."

The Examiner rejects claims 1 to 4, 23, 24, 26 to 31, 34 to 37 and 40 under 35 USC 102(b) as being anticipated by Woo (PNAS, Aug. 1978, vol 75, No. 8 p 3688 to 3692) and Woo (Biochem., 1981, vol 20, p 6437-6446). Applicant traverses the rejection.

The Examiner states that Woo (PNAS) taught a 2.4 kb, 1.8 kb and 9.5 kb fragment of the chicken ovalbumin gene. Applicant disagrees. The fragments described in Woo (PNAS) were not sequenced and therefore do not describe the claimed sequences and as such cannot anticipate the claims.

The Examiner indicates that Woo (Biochem.) taught what Woo believed to be the complete nucleotide sequence of 7564 nucleotides for the chicken ovalbumin gene and therefore anticipates the claims. Applicant disagrees. The sequence described in Woo (Biochem.) is only about 7.5 kb in length and therefore cannot anticipate SEQ ID NO: 1, which is about 195 kb in length.

In addition, the sequence of Woo (PNAS) does not describe the MARs of claim 76 and 77. The 7.5 kb sequence shown in FIGURE 2 at page 6440 of Woo (PNAS) is a sequence contiguous with the ovalbumin coding sequence. As can be seen in Fig. 1 of the application, the translation start site (ATG) of the ovalbumin coding sequence is at nucleotide 133382 of SEQ ID NO: 1. Therefore, the 7.5 kb sequence of Woo (PNAS) cannot reach into the MARs of claim 76 and 77 which are more than 90,000 nucleotides and 35,000 nucleotides away from the ovalbumin translation start site respectively.

The Examiner rejects claims 1 to 7, 23, 24, 26 to 31, 34 to 37 and 40 under 35 USC 102(b) as being anticipated by Schreiber (AC159826). Applicant traverses the rejection.

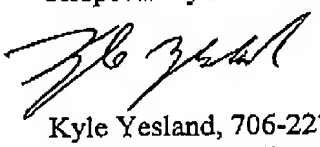
The Examiner states that Schreiber taught a BAC clone CH261-57J20, Accession Number: AC159826 that comprises SEQ ID NO: 1. The question of whether the sequence of AC159826 comprises claimed sequences need not be addressed since the sequence listing in AC159826 is not prior art to the subject case which was filed in 2003 and claims an even earlier priority date. The publication date for the sequence of AC159826 was in 2005. There is no mention of a 2001 submission date for AC159826 as the Examiner suggests. Furthermore, a submission date does not qualify as a prior art date under 35 USC 102(b).

In conclusion, applicant has shown that pending claims 1 to 4, 6 to 9, 23 to 26, 29 to 33, 35 to 39 and 72 to 77 meet the requirements for patentability and therefore, applicant submits that the claims are allowable and respectfully requests the Examiner to pass the above-identified application to allowance.

If any issues remain to be addressed in this matter, which might be resolved by discussion,

the Examiner is respectfully requested to call applicants' undersigned counsel at the number indicated below.

Respectfully submitted,



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